Remarks

Applicant appreciates the thorough examination of the present application as evidenced by the final Office Action mailed January 14, 2004 ("Final Office Action"). Claims 20-51 are pending in the present application. Claims 20-51 stand rejected. Applicant has cancelled claims 23, 24, 29, 31, 33, 34, 39 and 41-51, without prejudice. Applicant has further added new claims 52-55. Support for new claims 52-55 can be found in the specification at page 7, lines 18-22, among other places.

The concerns raised by the Examiner are addressed below.

I. Claim Rejection Under 35 U.S.C. § 102 in View of U.S. Patent No. 5,069,911 to Züger

Claims 20-23, 25-28, 30-38 and 40-49 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,069,911 to Züger ("Züger"). Applicant respectfully traverses this rejection.

The Final Office Action states the following:

> '911 teaches a sustained release combination of ergot derivatives such as α-dihydroergocryptine (col. 1, lin. 55-60) with hydrophilic swelling agents and pharmaceutical excipients such as hydroxypropylcellulose and beeswax (col. 2, lin. 30-55). The reference teaches a ratio of ergot derivative to hydrophilic swelling agent of 1:05 to 1:40 (col. 4, lin. 37-col. 5, lin. 25). The reference also teaches that α-dihydroergocryptine is present in the formulation in a concentration of 1-15 mg (col. 5, lin. 14-24). These disclosures render the claims anticipated.
>
> Final Office Action, page 2.

It is well accepted that "[a]nticipation under 35 U.S.C. § 102 requires the disclosure in a single piece of prior art of **each and every limitation of a claimed invention**." *Apple Computer Inc. v. Articulate Systems Inc.* 57 USPQ2d 1057, 1061 (Fed. Cir. 2000) (*relying on Electro Med. Sys. S.A. v. Cooper Life Scis.*, 32 USPQ2d 1017, 1019 (Fed Cir. 1994) (emphasis added). Applicant respectfully submits that each and every recitation of the present claims is not provided by Züger.

Claim 20 of the present application is directed to, among other things, a **method of improving bioavailability** of ergot derivatives administered using sustained-release delivery systems wherein, among other things, **the**

bioavailability is at least 25% higher than the bioavailability of an ergot derivative or mixture thereof administered using a conventional drug delivery system. Newly added claim 52 of the present application is directed a **method of improving bioavailability** of ergot derivatives administered using sustained-release delivery systems wherein, among other things, the ratio of α-dihydroergocryptine to hydrophilic swelling agent is about 1:1 to about 1:4.

In contrast, Züger proposes pharmaceutical 9,10-dihydrogenated ergot alkaloid containing compositions and methods for treating cerebral insufficience and disorder, hypertension or migraine (*See* claim 10) and methods for treating hypotension, orthostatic circulation disturbances or migraine (*See* claim 11). More specifically, Züger does not propose, among other things, a method of improving bioavailability of ergot derivatives administered using sustained-release delivery systems. Züger does not propose a method of improving bioavailability of ergot derivatives administered using sustained-release delivery systems wherein, among other things, **the bioavailability is at least 25% higher than the bioavailability of an ergot derivative or mixture thereof administered using a conventional drug delivery system**. Moreover, Züger does not propose a method of improving bioavailability of ergot derivatives administered using sustained-release delivery systems wherein, among other things, the ratio of α-dihydroergocryptine to hydrophilic swelling agent is about 1:1 to about 1:4.

In further support of the anticipation rejection, the Final Office Action refers to the ratio of the ergot derivative to hydrophilic swelling agent. More specifically, the Final Office Action incorrectly states that "[t]he reference [Züger] teaches a ratio of ergot derivative to hydrophilic swelling agent of 1:05 to 1:40." Final Office Action, pages 2-3. Instead, Züger proposes that the "[p]referred ratios of 9,10-dihydro ergot alkaloid to swelling substance are from about 1:4 to 1:50, e.g. 1:4 to 1:25." Züger, col. 4, lines 44-46. Züger further states that "[p]referably the ratio of dihydroergotamine to swelling substance is from 1:4 to 1:20, e.g. 1:5 to 1:20, especially from 1:4 to 1:12, e.g. from 1:5 to 1:12." Züger, col. 4, lines 66-68. Thus, as stated above, Züger does not teach a **method of improving bioavailability** of ergot derivatives administered using sustained-

release delivery systems wherein, among other things, the ratio of α-dihydroergocryptine to hydrophilic swelling agent is about 1:1 to about 1:4.

Accordingly, Applicant respectfully submits that claims 20, and claims that depend therefrom, and new claims 52 and 54 are not unpatentable under 35 U.S.C. § 102(b) in view of U.S. Patent No. 5,069,911 to Züger, and respectfully requests that this rejection be withdrawn.

II. Claim Rejection Under 35 U.S.C. § 102 in View of U.S. Patent No. 3,752,888 to Fluckiger et al.

Claims 20, 24-27, 29, 41 and 47 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 3,752,888 to Fluckiger et al. ("Fluckiger et al."). In an effort to expedite prosecution of the pending application, Applicant has amended claim 20 to delete the recitation directed to "bromocryptine." Additionally, Applicant has cancelled claims 24, 29, 41 and 47, without prejudice, and respectfully requests withdrawal of this rejection as being moot.

III. Claim Rejection Under 35 U.S.C. § 103 in View of U.S. Patent No. 3,752,888 to Fluckiger et al.

Claims 39 and 51 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Fluckiger et al. As previously noted, claims 39 and 51 have been cancelled, without prejudice, in order to expedite prosecution of the pending application. Accordingly, Applicant respectfully requests withdrawal of this rejection as being moot.

IV. Response to Amendment and Arguments

Applicant again acknowledges with appreciation the thorough examination provided by the Examiner as evidenced by the Examiner's response to Applicant's amendment and arguments.

Applicant reiterates that the Declaration Under 37 C.F.R. § 1.132 of Dr. Federico Mailland (the "Mailland Declaration") was submitted as a precautionary measure in response to the 35 U.S.C. § 103(a) obviousness rejection and not the § 102 anticipation rejection. Regarding the Mailland Declaration, the Final Office

Action states that the Mailland Declaration is "drawn to a specific example of an ergot derivative formulation, while the claims are drawn to a generic formulation. The examples of the declaration disclose specific concentrations, which are not represented in the instant claims." Final Office Action, page 5. As previously stated, the Mailland Declaration clearly shows that the ergot derivative sustained-release formulations of the present invention increase the bioavailability of the administered drug as compared to conventional delivery systems and as compared to the formulations disclosed by Züger. Applicant has added new claims 53 and 55 that further clarify embodiments of the formulations provided by the present invention.

Further, in the response to Applicant's arguments regarding 35 U.S.C. § 102, the Final Office Action states that Züger provides "ratios of ergot derivatives including dihydroergocryptine ranging from 1:4 to 1:25, which falls within the 1:0.5 to about 1:5 range of the instant claims." Final Office Action, page 6. As noted in the arguments presented above, Züger does not recite each and every recitation of the present claims as required to establish anticipation under 35 U.S.C. § 102.

V. Election/Restrictions

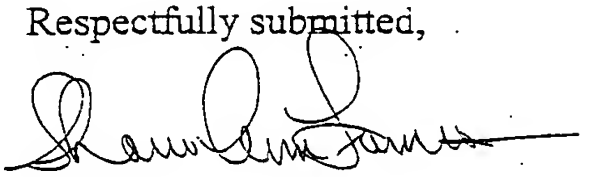
As a formality, Applicant hereby elects claims directed to α-dihydroergocryptine. Applicant has amended claim 20 to delete the recitation directed to "bromocriptine." Accordingly, claims 20-22, 25-28, 30, 32, 35-38, 40 and new claims 52-55 read upon the elected species.

Conclusion

With the concerns of the Examiner addressed in full, Applicant respectfully requests entry of this Amendment, withdrawal of the outstanding rejections, and the issuance of a Notice of Allowance forthwith. Alternatively, Applicant respectfully

requests entry of this Amendment as narrowing the issues for further consideration. The Examiner is encouraged to direct any questions regarding the foregoing to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,



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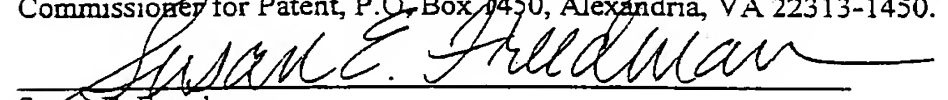

Susan E. Freedman
Date of Signature: February 23, 2004